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L2	Campbell-Joy-$.in.	2	L2
DB=USPT; THES=ASSIGNEE; PLUR=YES; OP=ADJ			
L1	Campbell-Joy-$.in.	1	L1

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INFORMATION FOR
HEALTH PROFESSIONALS

Data Sheet

INTRAGAM®

Normal Immunoglobulin (Human), For Intravenous Use

Description

Intragam® is a sterile, preservative free solution containing 6 g of human protein and 10 g of maltose in each 100 mL. Isotonicity is achieved by the addition of maltose. At least 98% of the protein has the electrophoretic mobility of immunoglobulin G (IgG). At least 90% of the protein is IgG monomer. There are also traces of IgA and IgM. The distribution of IgG subclasses is similar to that found in normal serum.

Intragam® is made by a cold ethanol fractionation of large pools of human plasma obtained from voluntary blood donors. The protein has not been chemically or enzymatically modified. However, the pH of the solution has been adjusted to pH 4.25. Intragam® is intended for intravenous administration.

Special Warning

When medicinal products prepared from human blood or plasma are administered, infectious diseases due to the transmission of infective agents cannot be totally excluded. This applies also to pathogens of hitherto unknown origin.

To reduce the risk of transmission of infective agents, stringent controls are applied to the selection of blood donors and donations. In addition, virus removal and inactivation procedures are included in the production process.

The current procedures applied in the manufacture of medicinal products derived from human blood or plasma are effective against enveloped viruses such as HIV (human immunodeficiency virus), hepatitis B and hepatitis C viruses.

These procedures are of limited value against non-enveloped viruses.

Vaccination for patients in receipt of medicinal products from human blood or plasma should be considered where appropriate.

Pharmacology

Intragam® supplies a spectrum of IgG antibodies against a wide variety of infective agents. As the product is administered intravenously, essentially 100% of the infused IgG antibodies are immediately

available in the recipient's circulation.

In immunodeficient children the half-life was found to be 21 to 42 days. In patients with a normal acid-base compensatory mechanism, the acid load delivered by the largest dose of the preparation would be neutralised by the buffering capacity of whole blood alone, even if the dose were to be infused instantaneously. (An infusion usually lasts several hours).

In patients with limited or compromised acid-base compensatory mechanisms, consideration should be given to the effect of the additional acid load that the preparation might present.

Indications

Intragam® is indicated in patients with primary immune deficiency syndromes for whom replacement of IgG is intended. Intragam® may also be of benefit as an alternative treatment for idiopathic thrombocytopenic purpura but conclusive evidence of efficacy is lacking for this indication at the present time.

Contraindications

Intragam® is contraindicated in individuals who have had a true anaphylactic reaction to a human immunoglobulin preparation. Individuals with selective IgA deficiency should not receive the preparation, since these patients may develop antibodies to IgA and experience severe reactions to IgA which is present in Intragam® in trace amounts.

Warnings and Precautions

Intragam® should only be administered intravenously. Other routes of administration have not been evaluated. It is possible that Intragam® may, on rare occasions, cause a precipitous fall in blood pressure and a clinical picture of anaphylaxis. Therefore, adrenaline and oxygen should be available for the treatment of such an acute reaction.

An aseptic meningitis syndrome (AMS) has been reported to occur infrequently in association with Intravenous Immunoglobulin (Human) (IVIG) treatment. The syndrome usually begins within several hours to two days following IVIG treatment. It is characterised by symptoms and signs including severe headache, nuchal rigidity, drowsiness, fever, photophobia, painful eye movements, and nausea and vomiting. Cerebrospinal fluid (CSF) studies are frequently positive with pleocytosis up to several thousand cells per cu. mm., predominantly from the granulocytic series, and elevated protein levels up to several hundred mg/dl. Patients exhibiting such symptoms and signs should receive a thorough neurological examination, including CSF studies, to rule out other causes of meningitis. AMS may occur more frequently in association with high dose (2 g/kg) IVIG treatment. Discontinuation of IVIG treatment has resulted in remission of AMS within several days without sequelae.

Positive direct antiglobulin tests and red cell haemolysis have been reported following high dose infusion of intravenous immunoglobulin due to the presence of anti-A, anti-B, and occasionally anti-D or other erythrocyte antibodies in the product. Such red cell sensitisation may cause crossmatching

difficulties and transient haemolytic anaemia.

Prolonged administration (over 6 hours) using large doses (greater than 400 mg/kg) may result in thrombophlebitis at the infusion site.

If the product appears to be turbid by transmitted light or contains any sediment, it must not be used, and the bottle should be returned unopened to the Blood Transfusion Service. **Intragam® contains no antimicrobial agent.** It must, therefore, be used immediately after opening the bottle; any unused portion should be discarded. Do not use if the solution has been frozen.

Intragam® may be diluted with up to 4 parts of 0.9% saline or 5% glucose. No other drug interactions or compatibilities have been evaluated. Intragam® should be administered separately from other intravenous fluids or medications the patient might be receiving. Allow the preparation to reach room temperature before infusing into the patient.

There have been occasional reports of renal dysfunction and acute renal failure in patients receiving intravenous immunoglobulin (IVIG) products. Patients at increased risk are those with pre-existing renal insufficiency, diabetes mellitus, age greater than 65 years, volume depletion, sepsis and paraproteinaemia, and those taking concomitant nephrotoxic drugs. The majority of such incidents have been associated with sucrose-containing products. Whilst there is no sucrose in Intragam® the following precautions should be followed.

Patients should be adequately hydrated prior to the initiation of the IVIG infusion and the recommended dose should not be exceeded. Renal function should be monitored in patients at increased risk of developing acute renal failure. If renal function deteriorates, discontinuation of IVIG should be considered.

Use In Pregnancy

The safety of this medicinal product for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given with caution to pregnant women. Long lasting clinical experience with immunoglobulins, indicates that no harmful effects on the course of pregnancy or on the foetus are to be expected.

Use In Lactation

The safety of this medicinal product for use during lactation has not been established in controlled clinical trials and therefore should only be given with caution to breast-feeding mothers. Long lasting clinical experience with immunoglobulins, indicates that no harmful effects on the neonate are to be expected.

Immunoglobulins are excreted into the milk and may contribute to the transfer of protective antibodies to the neonate.

Adverse Reactions

Reactions to intravenous immunoglobulin tend to be related to the infusion rate and are most likely to occur during the first hour of the infusion. It is recommended that the patient's vital signs and general

status be monitored regularly throughout the infusion.

The types of reactions that may occur include: abdominal pain, headache, chest-tightness, facial flushing or pallor, hot sensations, dyspnoea, non-urticarial skin rash, itching, hypotension, nausea, or vomiting. Should any of these reactions develop during infusion of Intragam®, the infusion should be temporarily stopped until the patient improves clinically (5 to 10 minutes) and then cautiously recommenced at a slower rate.

Some patients may develop delayed adverse reactions to Intragam® such as: nausea, vomiting, chest pain, rigors or aching legs. These adverse reactions occur after the infusion has stopped but usually within 24 hours.

True hypersensitivity reactions to intravenous immunoglobulin such as urticaria, angioedema, bronchospasm or hypotension occur very rarely. Should an anaphylactic reaction to Intragam® develop, the infusion should be stopped and treatment instituted with adrenaline, oxygen, antihistamine and steroids.

Neutropenia has been reported in rare instances in association with Intragam® and other normal immunoglobulin products. Antineutrophil antibodies have been detected in some batches of Intragam® but their clinical significance is unclear.

Haemolytic anaemia has been reported (see **Warnings and Precautions**). Mild and moderate elevations of serum transaminases (AST, ALT, gamma GT) have been observed in a small number of patients given Intragam®. Such changes were transient and not associated with the transmission of hepatitis.

There have been reports that intravenous immunoglobulin can affect renal function. This should be monitored in patients with pre-existing renal failure who are given Intragam®. Rarely, renal dysfunction and acute renal failure have been reported (See **Warnings and Precautions**).

Dosage and Administration

A patient with an extremely low serum IgG concentration requires 400 mg IgG per kilogram body weight initially, followed by monthly maintenance doses of at least 200 mg per kilogram body weight. Often the maintenance dose is between 300 and 450 mg of IgG per kilogram body weight. As catabolic rates vary, the IgG levels of each new patient should be monitored regularly for several monthly cycles, to determine the effective dose for that individual. While the minimum level of IgG required for protection against infections has not been determined, the following levels represent the 5th percentile in a population of children attending a hospital in Melbourne, Australia:

Age	5th percentile	
(years)	mg/100 mL	IU/mL
1 to <2	350	40
2 to <4	435	50
4 to <6	520	60
6 to <9	565	65
>9	610	70

Intragam® may be infused undiluted. Intragam® may also be infused diluted with up to 4 parts of 0.9% saline or 5% glucose. The infusion may be commenced at the rate of 1 mL per minute. After 15 minutes

the rate may be gradually increased to a maximum of 3 to 4 mL per minute over a further 15 minutes. The volume and acid load should be considered if Intragam® is administered to neonates.

Instructions for use

Intragam® may be administered through any standard I.V. infusion giving set. The following procedure is recommended:

1. Remove the dust cover from the top of the bottle of Intragam®.
2. **Apply a suitable antiseptic such as povidone-iodine solution or 70% ethanol to the exposed part of the rubber stopper and allow to dry.**
3. Stand the bottle upright and insert the air vent needle vertically in one of the outer indentations of the stopper. It is preferable to use a long airway needle fitted with a filter. If not available, a short needle attached to a non-wettable filter may be used.
4. Clamp the tubing of the giving set and insert the needle at the upper end of the giving set vertically through the central indentation of the stopper.
5. Invert the bottle and attach the hanger to a support approximately one metre above the patient.
6. Allow the tubing to fill by adjusting the clamp. Insert the giving set needle into a vein and adjust the rate of flow.
7. When the bottle is empty, clamp the tubing and transfer the air vent needle and the needle at the upper end of the giving set to a further bottle of Intragam® or to a bottle containing a crystalloid solution, according to requirements.

Overdosage

No information available.

Presentation

This product is available in 50, 200, and 500 mL bottles containing 3, 12, and 30 g of IgG and 5, 20, and 50 g of maltose respectively.

No antimicrobial agent added.

Storage

Store at 2°C to 8°C (Refrigerate. Do not freeze.) Protect from light.

Name and Address

Name and Address of Sponsor

CSL (New Zealand) Limited
PO Box 62590
Central Park
Auckland
NEW ZEALAND

Name and Address of Manufacturer

CSL Limited ACN 051 588 348
at: 189-209 Camp Road
Broadmeadows 3047 VIC
AUSTRALIA

Name and Address of Distributor

New Zealand Blood Service Limited
169 Manukau Road
Epsom
Auckland
NEW ZEALAND

Date of Preparation

28 October 1999

Intragam® is a registered trademark of CSL Limited.

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                   E CAMPBELL JOY?/AU
L2              18 S E1 OR E2
L3               2 S STROHBEHN RONALD?/AU
                   E STROHBEHN RONALD?/AU
L4               2 S E1 OR E2
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L5              11 S E1 OR E2
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                   E POLO POZO FRANCISCO?/AU
L7         9858920 S E1 OR 22
L8               2 S E1 OR E2
                   E ARTHINGTON JOHN?/AU
L9               1 S E1 OR E1
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L10             16 S E1 OR E2
L11          12533 S L1 (S) (VIVO OR ADMINISTER?) (S) (BLOOD OR EGG OR MILK)
L12           9107 S L11 (S) (CHRONIC FATIGUE SYNDROME OR IMMUNO?)
L13              0 S L12 (S) ( IGG SAME DEFICIEN?)
L14            226 S L12 (S) ( IGG (S) DEFICIEN?)
L15             75 DUP REM L14 (151 DUPLICATES REMOVED)

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